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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,972	SCHWAB ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *114-132* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *114-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *18 March 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 18 March 2005 has been entered.

2. Claims 114 – 132, which were allowed in the examiner's amendment mailed 28 October 2004, are pending and under examination. Authorization for the examiner's amendment was given in a telephone conversation between Adriane Antler and Christopher Nichols on 13 October 2004.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

4. Claims 114 – 119 and 123 – 125 are objected to because of the following informalities:

Claims 114 – 116 recite both SEQ ID NO:2 and residues 1 – 1163 of SEQ ID NO:2. SEQ ID NO:2 has 1163 amino acids, and therefore it is not apparent how these two members of the Markush group can be distinguished from one another. Similarly claims 117 – 119 recite both SEQ ID NO:29 and residues 1 – 1178 of SEQ ID NO:29, but since SEQ ID NO:29 has exactly 1178 residues, it is not clear how these two members of the Markush group can be distinguished from one another.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

5. Claims 114, 116 – 129, and 131 – 132 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for full-length proteins and fusions proteins which inhibit spreading of NIH3T3 fibroblasts or PC12 cells (i.e. SEQ ID NO:2, SEQ ID NO:29, residues 1 – 171 of SEQ ID NO:2 fused to residues 975 – 1163 of SEQ ID NO:2, residues 1-172 of SEQ ID NO:29 fused to residues 990-1178 of SEQ ID NO:29), and for isolated host cells,

does not reasonably provide enablement for those fragments claimed that do not inhibit fibroblast spreading (i.e. residues 975 – 1163 of SEQ ID NO:2, residues 990 – 1178 of SEQ ID NO:29, and SEQ ID NO:32), or for all recombinant host cells, or for all mammalian proteins, or for all human proteins, or for all nucleic acids which hybridize under stringent conditions as defined in claim 127. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses (p. 68 and Figure 13) that Nogo-C, which comprises the carboxy-terminus of the peptide (i.e. amino acids 975 – 1163 of SEQ ID NO:2) does not inhibit spreading in the fibroblast assay. The table presented on page 68 clearly indicates that Nogo-C is not active in the assay, and the final sentence indicates that it can be removed without loss of inhibitory activity. Since inhibitory activity in the NIH 3T3 fibroblast assay *is* Nogo activity as defined on page 11 lines 25 – 30 of the specification, applicant has not shown how to use this fragment of SEQ ID NO:2. Since residues 975 – 1163 of SEQ ID NO:2 correspond to residues 990 – 1178 of SEQ ID NO:29 (specification, page 30, lines 26 – 31), applicant has also not disclosed how to use that fragment.

The specification discloses (p. 8, lines 8 – 9) that SEQ ID NO:32 is rat Nogo-C. However the results of the working example presented in Figure 18 and on page 68 of the specification clearly indicate that Nogo-C does not inhibit spreading in the fibroblast assay. Applicant has not shown how to use SEQ ID NO:32, because the specification clearly shows that Nogo-C does not work in the 3T3 spreading assay. Furthermore the specification does not provide sufficient guidance to allow a skilled artisan to make and use polypeptides at least 90% identical to SEQ ID NO:32 which *do* have Nogo activity, i.e. applicant has not shown which residues must be inserted, deleted, or changed to confer Nogo activity onto SEQ ID NO:32.

35 USC 112 first paragraph requires that the disclosure show how to both make and use the claimed invention. In the instant case, applicant has not shown how to use the invention, and clearly has not met the requirements of the statute. Therefore claims 114 and 116 – 119 are rejected. Claim 125 is depends from these claims and therefore is also rejected. Claims 126 – 132 are drawn to nucleic acids encoding proteins of claims 114 and 116 – 122, as well as vectors, host cells, and methods of making protein and are rejected for the same reasons. Since applicant has not shown how to use the claimed fragments of protein, there is not a use for the nucleic acids encoding said proteins.

The specification discloses (p. 30, lines 26 – 31) that the region comprising residues 940 – 1127 of SEQ ID NO:29 corresponds to residues 975 – 1163 of SEQ ID NO:2. But claims 117 – 119 recite residues 990 – 1178 of SEQ ID NO:29, both alone and as part of fusion proteins. Applicant has not demonstrated how to use fragments comprising residues 990 – 1178 of SEQ ID NO:29, and it is unclear which are the corresponding residues in SEQ ID NO:2.

The specification discloses that SEQ ID NO:29 is a human protein, and that SEQ ID NO:2 and SEQ ID NO:32 are both rat proteins. Claim 123 is drawn to any of claims 114 – 122, wherein the protein is mammalian. The only mammalian proteins which applicant has taught how to make are SEQ ID NO:2 and 29. SEQ ID NO:32 is not a mammalian protein, it is a fragment of a mammalian protein. Furthermore the fusion proteins recited in claims 114 – 119 are not mammalian proteins; they are artificially-created proteins, made in the laboratory, which are based upon mammalian sequences. Claim 124 is drawn to any of claims 114 – 122, wherein the protein is human. Only the full-length human protein (i.e. SEQ ID NO:29) is human. Other proteins are either mutants based on the human sequence (i.e. the fusion between the N- and C-terminal regions of SEQ ID NO:29, as well as proteins related by sequence identity but which do not exist in nature, as well as the C-terminal fragments of SEQ ID NO:29), or are based on rat sequences. Applicant has not shown how to make any protein other than SEQ ID NO:29 wherein the protein is human.

Claim 127 is drawn to nucleic acids which hybridize to certain nucleic acids under certain hybridization conditions. There is no requirement that the nucleic acids which hybridize have any particular function, or be of any length at all, or that they encode a functional protein. The art recognizes that the conditions for washing are as important in determining the specificity of a hybridization experiment as the conditions of hybridization themselves. The exact washing conditions have enormous influence on the results of any library-screening experiment; see particularly Strauss (1993. Current Protocols in Molecular Biology), who teaches that washing temperature and salt concentration influence hybridization stringency (p. 6.3.6). With these points in mind, it is the Examiner's position that giving the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement. Applicant has not shown how to make and use a representative number of different sequences which fall within the scope of claim 127. In the absence of sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims.

Claims 129 and 131 are drawn to host cells comprising vectors encoding Nogo proteins. The broadest reasonable interpretation of this claim includes host cells residing in transgenic animals and host cells residing in humans wherein the cells have been genetically modified by the administration of a nucleic acid. The specification appears to contemplate both gene therapy (see p. 38 line 36 – p. 42 – line 17) and genetically modified organisms (p. 55 line 11 - 31). However there is not sufficient guidance in the specification that would allow a skilled artisan to make and use a transgenic animal comprising any of the instantly claimed nucleic acids, or how to successfully use the claimed nucleic acids in recombinant gene therapy methods.

Those skilled in the art recognize that such technology is currently beyond scope. In particular, Marshall "Gene Therapy's Growing Pains". Science, Vol. 269 (1995), pp. 1050-1055, and Verma, I. M., et al. "Gene therapy-promises, problems, and prospects". Nature, Vol. 389 (September 1997), pp. 239-242, and Orkin et al. (1995) "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" all denote significant troubles associated with transgenic and in vivo gene therapy approaches to the assessment of in vivo methods and treatments.

The specification fails to provide any exemplary evidence for conducting such screening approaches in vivo, using either transgenic or gene therapy treated cells within an organism. Since the scope of "host cell" is deemed to be so inclusive as provided by guidance within the specification, the scope of enablement provided by the specification is not commensurate in scope with the claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Amendment to "isolated" cells is recommended.

6. Claims 115 – 116, 118 – 119, and 121 – 132 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 115 – 116, 118 – 119, and 121 - 122 are drawn to proteins at least 90% and 95% identical to disclosed SEQ ID NO:s or specific fragments thereof, wherein the protein has Nogo activity. Applicant has defined Nogo activity (specification, p. 11, lines 22 – 31) very broadly and has included both antigenicity and immunogenicity within this definition. Applicant has not described the common structural elements, present in all members of the genus, which are required such that the resulting protein has the desired properties. Because applicant has not disclosed either a representative number of members falling within the genus or a description of the structural elements common to all members of the genus, the claims do not meet the written description requirement.

Claims 123 and 124 are drawn to any of the proteins in claims 114 – 122 which is mammalian or human, respectively. But the only proteins which are mammalian are SEQ ID NO:2 and 29, and the only protein which is human is SEQ ID NO:29. Applicant has not shown possession of any other human proteins other than SEQ ID NO:29, or any mammalian proteins other than SEQ ID NOS: 2 and 29. Those proteins which are either fragments, fusion proteins, or proteins related by sequence identity to SEQ ID NO:2 and 29 are not mammalian, because they do not occur in mammals.

Claim 127 is drawn to a broad genus of nucleic acid sequence which are not limited by sequence, length, or function other than they have to hybridize to certain other nucleic acids. The examiner acknowledges that the hybridization conditions recited appear on p. 13 lines 35 – 36 of the specification. However the claim does not recite any washing conditions, and the art teaches that the salt concentration and temperature of the washes have enormous influence on the results of a hybridization experiment. Applicant has not provided a sufficient number of examples of nucleic acid sequences which fall within the scope of this claim to allow the examiner to conclude that he did in fact have possession of this genus whose breadth appears to be unlimited in the absence of structural limitations or explicit recitation of washing conditions.

7. Claims 117 – 119 and 121 - 132 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 117 – 119 recite residues 990 – 1178 of SEQ ID NO:29. The examiner has not found support for this fragment in the specification, drawings, or claims as originally filed. Page 30, lines 18 – 31 appear to provide support for the fragment from residues 940 – 1127 of SEQ ID NO:29, but not for instantly-claimed 990 – 1178. There does not appear to be contemplation of residues 990 – 1178 in the original specification.

Claims 121 – 122 are drawn to proteins at least 90% or 95% identical to SEQ ID NO:32 which have Nogo activity. While the specification contemplates proteins 90% or 95% identical to all claimed proteins (see p. 31, line 26), there does not appear to be contemplation of proteins related by identity to SEQ ID NO:32 and have a property which it does not have, namely Nogo activity.

Claims 123 and 124 are drawn to any of the proteins in claims 114 – 122 which is mammalian or human, respectively. But the only proteins which are mammalian are SEQ ID NO:2 and 29, which are the rat and human sequences respectively. There is no contemplation in the specification to broaden the scope of these proteins to encompass the sequences to mammals as broadly recited in claim 123. Original claims 9 and 10 appear to indicate contemplation of certain proteins, namely those based on the human sequence, as human proteins, and other proteins, also those based on the human sequence, as mammalian proteins. There does not appear to be contemplation of proteins which are not the human sequence being given human properties, nor does there appear to be contemplation of proteins related by sequence identity to any of SEQ ID NOS:2, 29, or 32 as mammalian or human proteins. The specification as originally filed does not provide support the additional functional limitations.

Claim Rejections - 35 USC § 112, second paragraph

8. Claims 115 – 116, 118 – 119, 123 – 125, and 127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 115 recites the limitation "90% or greater sequence identity with amino acids 1 – 171 fused to amino acids 975 – 1163 of SEQ ID NO:2". Claim 116 recites the same verbiage but the limitation is 95% identity. Claims 118 – 119 recite similar verbiage, but are drawn to slightly different residues of SEQ ID NO:29. The claims are all indefinite for the same reason. It

is unclear whether the 90% or 95% limitation applies to the N-terminal fragment, for example residues 1 – 171 of SEQ ID NO:2, or if the limitation refers to the entire fusion construct. Therefore a skilled artisan would not be able to determine the metes and bounds of claims 115 – 116 and 118 – 119. Claims 123 – 125 are rejected because they depend from a rejected base or intermediate claim.

Claims 123 are drawn to proteins which are mammalian or human, but refer to sequences which are neither. For example, both claims depend from claim 11, which includes the polypeptide comprising amino acids 1 – 171 fused to 975 – 1163 of SEQ ID NO:2. This is neither a human nor mammalian protein; it is a deletion mutant based on a rat sequence. Therefore the claims are unclear.

Claim 127 contains the trademark/trade name Ficoll. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a nonioninc sucrose solution and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

Priority Determination

9. 35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

10. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. As detailed in the new matter rejection

under 35 USC § 112, first paragraph above, neither the specification as originally filed nor provisional application 60/107,446 provides support for the specific fragments of SEQ ID NO:29 claimed herein (i.e. residues 990 – 1178). Therefore, the effective filing date for claims 117 – 119 and 123 – 132 is the instant filing date, 24 September 2001. The effective filing date for claims 114 – 116 and 120 – 122 is the date the provisional application was filed, 6 November 1998.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claim 127 is rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene random primers, 1991 catalog, p. 66.

Stratagene teaches random 9-mers capable of hybridizing with all possible gene sequences. The random primers meet the claim limitations because the primers are a complement to SEQ ID NO:2, 29, and 32 and are able to bind under stringent hybridization conditions as defined in claims 127. It is noted that the claim does not recite washing conditions and therefore the random primers will remain hybridized to the target sequence. Thus, the reference teachings anticipate the claimed invention.

13. Claims 115 – 116 and 125 – 132 are rejected under 35 U.S.C. 102(e) as being anticipated by Bandman et al. (U.S. Patent 5,858,708, issued 12 January 1999, filed 12 August 1996). Bandman et al. teach SEQ ID NO:1. Residues 12 – 199 of Bandman et al.'s SEQ ID NO:1 are 97.7% identical to residues 976 – 1163 of applicant's SEQ ID NO:2. Bandman et al. also teach SEQ ID NO:2, which is a nucleic acid that encodes said protein. Bases 108 – 671 of Bandman's SEQ ID NO:2 encode a peptide 97.7% identical to residues 976 – 1163 of applicant's SEQ ID NO:2, meeting the limitations of claim 126. Because a nucleic acid will

hybridize to its own complement under stringent conditions, the sequence from Bandman will hybridize to the complement of SEQ ID NO:2 and therefore also meets the limitation of claim 127. Bandman et al. teach vectors and host cells comprising said nucleic acid as well as methods of making the protein using a recombinant host cell (see column 7 line 45 – column 11 line 26), meeting the limitations of claims 125 and 128 – 132. While Bandman et al. are silent as to the Nogo activity, the activity of the protein is an inherent characteristic and because the sequence meets the structural limitation of the claim it is assumed to meet the functional limitation as well.

14. Claims 118 – 119 and 125 – 132 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandman et al. Residues 12 – 199 of Bandman et al.'s SEQ ID NO:1 are 99.6% identical to residues 990 – 1178 of applicant's SEQ ID NO:29, recited in claims 118 - 119. Bandman et al. also teach SEQ ID NO:2, which is a nucleic acid that encodes said protein. Bases 108 – 671 of Bandman's SEQ ID NO:2 encode a peptide 99.57% identical to residues 990 – 1178 of applicant's SEQ ID NO:29, meeting the limitations of claim 126. Because a nucleic acid will hybridize to its own complement under stringent conditions, the sequence from Bandman will hybridize to the complement of bases 990 – 1178 of SEQ ID NO:29 and therefore also meets the limitation of claim 127. Bandman et al. teach vectors and host cells comprising said nucleic acid as well as methods of making the protein using a recombinant host cell (see column 7 line 45 – column 11 line 26), meeting the limitations of claims 125 and 128 – 132. While Bandman et al. are silent as to the Nogo activity, the activity of the protein is an inherent characteristic and because the sequence meets the structural limitation of the claim it is assumed to meet the functional limitation as well.

15. Claims 115 – 119, 123, and 125 – 132 are rejected under 35 U.S.C. 102(e) as being anticipated by Michalovich et al. (U.S. Patent Application Publication 2002/0010324, published 24 January 2002, effective filing date 22 July 1999, claiming benefit of foreign priority to 22 July 1998). Michalovich et al. teach SEQ ID NO:2. Residues 975 – 1163 of applicant's SEQ ID NO:2 are 98% identical to residues 1004 – 1192 of Michalovich's SEQ ID NO:2, meeting the limitations of claims 115 - 116. Residues 1 – 1192 of Michalovich's SEQ ID NO:2 are 98.1% identical to applicant's SEQ ID NO:29, meeting the limitations of claims 118 and 119. This sequence is 100% identical over the final 189 residues (i.e. residues 990 – 1178, recited in claims 117 – 119). Michalovich et al. teach SEQ ID NO:6. Residues 1 – 373 of their SEQ ID

NO:6 are 99.1% identical to residues 1 – 172 fused to 990 – 1178 of applicant's SEQ ID NO:29, meeting the limitations of claims 118 – 119.

Michalovich et al. also teach SEQ ID NO:5, a nucleic acid sequence. Bases 556 – 1119 of Michalovich's SEQ ID NO:5 encode a protein 97.7% identical to residues 975 – 1163 of applicant's SEQ ID NO:2; and bases 1 – 1119 of Michalovich's SEQ ID NO:5 encode a protein 98.9% identical to residues 1 – 172 fused to 990 – 1178 of SEQ ID NO:29, meeting the limitations of claim 126. Michalovich et al. also teach SEQ ID NO:1, which encodes a protein 98% identical to applicant's SEQ ID NO:29. Since the nucleic acid sequences of Michalovich et al. will hybridize to the complement of SEQ ID NO:2, the prior art sequences also meet the limitation of claims 127.

Michalovich et al. also teach expression systems (i.e. vectors) comprising the sequences, host cells comprising said vectors, and methods of making the protein recombinantly (see p. 4 paragraph 0065 – 0068), meeting the limitations of claims 125 and 128 – 132. While Michalovich et al. are silent as to the Nogo activity, the activity of the protein is an inherent characteristic and because the sequence meets the structural limitation of the claim it is assumed to meet the functional limitation as well.

16. Claims 117 – 119, and 123 – 127 are rejected under 35 U.S.C. 102(e) as being anticipated by Eiesenbach-Schwartz et al. (U.S. Patent Application Publication 2002/0072493 published 13 June 2002, filed 28 June 2001). On pages 22 – 23 of the remarks filed 19 August 2004, applicant indicates that the publication by Eisenbach-Schartz et al. is only entitled to 28 June 2001 as an effective filing date, as it is a continuation-in-part of several other applications, and the parent applications (i.e. 09/314,161, 09/218,277, and PCT/US98/14715) do not disclose the relevant nucleic acid and protein sequences. The examiner agrees; the effective filing date of the publication by Eisenbach-Schwartz is 28 June 2001. Applicant is reminded that the effective filing date for claims 117 – 119 and 123 – 132 is the instant filing date, 24 September 2001.

Eisenbach-Schwartz et al. teach SEQ ID NO:23. Residues 1004 – 1192 of their sequence is identical to residues 990 – 1178 of SEQ ID NO:29, meeting the limitations of claims 117 – 119. Residues 1 – 1192 of their SEQ ID NO:23 are 98.1% identical to applicant's full-length SEQ ID NO:29. This is a human sequence and thus also meets the limitations of claim 123 and 124. Eisenbach-Schwartz et al. also teach SEQ ID NO:22, a nucleic acid which encodes this protein. Their SEQ ID NO:22 encodes a protein 98.1% identical to SEQ ID NO:29.

Bases 3010 – 3576 of their SEQ ID NO:22 encode the C-terminal fragment (i.e. residues 990 – 1178). Thus the nucleic acid sequence from Eisenbach-Schwartz et al. meets the limitations of claim 126. Since the prior art sequence will hybridize to the complement of this nucleic acid, the reference also meets the limitations of claim 127. Claim 125 is a product-by-process claim, and since Eisenbach-Schwartz et al. teach the product claim 125 is also rejected.

Eisenbach-Schwartz et al. also teach SEQ ID NO:24. Residues 1 – 373 of their SEQ ID NO:24 are 99.1% identical to residues 1 – 172 fused to 990 – 1178 of applicant's SEQ ID NO:29, meeting the limitations of claims 118 – 119. This is a human protein and thus meets the limitations of claims 123 – 125 as well.

17. Claims 118 – 119 and 123 – 125 are rejected under 35 U.S.C. 102(e) as being anticipated by Cao et al. (US Patent Application Publication 2002/0034800, published 21 March 2002, effective filing date 16 December 1998, claiming benefit of provisional applications filed 30 December 1997, 24 September 1998, and 30 September 1998). Cao et al. teach SEQ ID NO:6. Residues 1 – 373 of their SEQ ID NO:6 are 99.1% identical to residues 1 – 172 fused to 990 – 1178 of applicant's SEQ ID NO:29, meeting the limitations of claims 118 – 119. Cao et al. teach that this is a human sequence, meeting the limitations of claims 123 and 124. Claim 125 is a product-by-process claim and since Cao et al. teach the product claim 125 is rejected as well.

18. Claims 126 - 128 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank AA986233, publicly available on 28 May 1998. GenBank AA986233 is a 718 base-pair nucleic acid; bases 20 – 433 encode a protein which is 90.14% identical to SEQ ID NO:32 (see enclosed alignment). The reference discloses that the sequence was inserted into pME18S-FL3 vector, thereby meeting the limitations of claims 126 and 128. Because the sequence will hybridize to its own complement under stringent conditions, the sequence also meets the limitation of claim 127.

19. Claims 126 – 127 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank AF132047, publicly available on 18 May 1999. Bases 180 – 1298 of AF132047 encode a protein 98.9% identical to residues 1 – 172 fused to residues 990 – 1178 of SEQ ID NO:29. Since the prior art sequence will hybridize to the complement of this nucleic acid, the reference also meets the limitations of claim 127.

20. Claims 126 and 127 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank AB015639, publicly available on 3 September 1999. GenBank AB015639 encodes a

protein 98.7% identical to residues 1 – 172 fused to 990 – 1178 of SEQ ID NO:29. Since the prior art sequence will hybridize to the complement of this nucleic acid, the reference also meets the limitations of claim 127.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 128 – 132 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of GenBank loci AA986233 or AF132047 or AB015639 or Eisenbach-Schwartz et al., each in view of Schendel 1998. Current Protocols in Molecular Biology 16.1.1 – 16.1.3). As detailed above, AA986233 and AF132047 and AB015639 and Eisenbach-Schwartz all teach nucleic acids which meet the limitations of claim 126. None of AA986233 and AF132047 and AB015639 and Eisenbach-Schwartz et al. teach nucleic acids in host cells comprising or methods of making protein recombinantly. Furthermore AF132047 and AB015639 and Eisenbach-Schwartz et al. do not teach vectors.

Schendel teaches methods of making protein recombinantly, using E. coli as the host cell and teaches vectors which are suitable for such purposes (see p. 16.1.1, bottom of first column). It would have been obvious to one of ordinary skill in the art to insert the nucleic acids of AA986233 or AF132047 or AB015639 or Eisenbach-Schwartz et al. into vectors, put those vectors in host cells, and make protein from the host cells, as taught by Schendel, with a reasonable expectation of success. A motivation to do so would be to produce large quantities

of the protein, which is then useful for making antibodies for detection or purification. Schendel teaches that the E. coli system offers advantages including ease of manipulation and low cost.

24. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1) Jacobs et al. WO 98/17687. Jacobs teach SEQ ID NO:8. Bases 1476 – 2027 of Jacobs encode a protein 94.22% identical to residues 975-1163 of SEQ ID NO:2.

2) Cocks et al. U.S. 6,607,879, issued 19 August 2003, filed 9 February 1998. Cocks et al. teach SEQ ID NO:382. Bases 1311 – 1875 encode a protein 96.32% identical to residues 975 – 1163 of SEQ ID NO:2 and 98.17% identical to residues 990 – 1178 of SEQ ID NO:29.

Conclusion

25. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 24, 2005

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